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Letter to the Editor: "Multiple Central Nervous System Hemangioblastomas"

The paper by Padovan and colleagues [1] describes a difficult aspect of Von Hippel Lindau syndrome to manage. The tendency to develop multiple hemangioblastomas, either metachronous or synchronous (and frequently both) and usually within the cerebellum, provides an enormous challenge to the treating clinician. As the authors say, this development has frequently proved fatal in the past. The new imaging techniques have thus far only allowed us to anticipate future problems, by showing the nascent next tumor(s), not to solve them.

While the Padua workers correctly draw attention to the radiosurgical report from Stanford [2], I believe their discussion underestimates the importance of radiotherapy as a whole in the management of this condition.

Sung et al. [3] reported a series of patients treated with conventionally fractionated radiotherapy and reported good responses, particularly in patients treated to doses greater than 4,000 cGy. Smalley et al. [4] came to similar conclusions, but found higher local control rates with doses of conventionally fractionated radiation above 5,000 cGy. We have also observed partial responses of central nervous system hemangioblastoma to similarly fractionated radiation [5].

Page et al. [2] described the treatment of 11 hemangioblastomas in 4 patients by radiosurgery, a technique of radiotherapy which delivers high single doses of radiation to highly discrete foci in the brain and which causes good obliterative results in other vascular tumors (notably arteriovenous malformations) for which conventionally fractionated radiation does not seem to be so effective. The hemangioblastomas varied in diameter from 0.75 to 2.0 cm and the radiosurgery single fraction dose from 3,000 to 7,500 cGy (mean 3,500 cGy) at the tumor margin—a remarkably high dose range at this prescription point—compared to arteriovenous malformation treatment dosage. The authors found that the tumors were controlled in all 11 cases. Our own recently reported observations in 6 such tumors (in 5 patients) are in agreement with those of the Stanford group [5], although we employed a lower radiosurgery dose (albeit sometimes in combination with conventionally fractionated radiation—vide infra).

From the literature cited above, coupled with our own observations, we have suggested that the optimal management of patients presenting with multiple hemangioblastomas in the cerebellum, as part of the Von Hippel Lindau syndrome, is the following: surgery to any large single tumor mass lesion, followed by conventionally fractionated radiotherapy to the whole cerebellum (and a parallel opposed pair of MV photon portals—the anterior border of which excludes the vast majority of the brainstem and runs parallel to the clivus so that the anterior brainstem is protected throughout the portal—would seem best) to a dose of 4,500–5,000 cGy. Some (perhaps 6) months later, a repeat magnetic resonance imaging (MRI) scan is performed: any persisting enhancing lesions are treated with radiosurgery to the lower dose that we have reported (Fig. 1) [5]. Our early observations support the notion that such an approach will allow the conventionally fractionated treatment course to obliterate early and subclinical disease, while leaving the less easily radiocurable lesions to radiosurgery (perhaps with smaller treatment volumes, due to some shrinkage following the first radiotherapy course).

Although the whole cerebellum receives external beam radiotherapy with this treatment strategy, the method of administration is perceived to be well within tolerance, and is a well-used treatment schedule in the management of other cerebellar tumors. Furthermore, we hope that this strategy will reduce the future operation rate and the need for multiple radiosurgery treatments in this group of children/young adults. Certainly Page et al. [2] found that the need for several radiosurgical treatment volumes within the same cerebellum increased the normal tissue morbidity rate.

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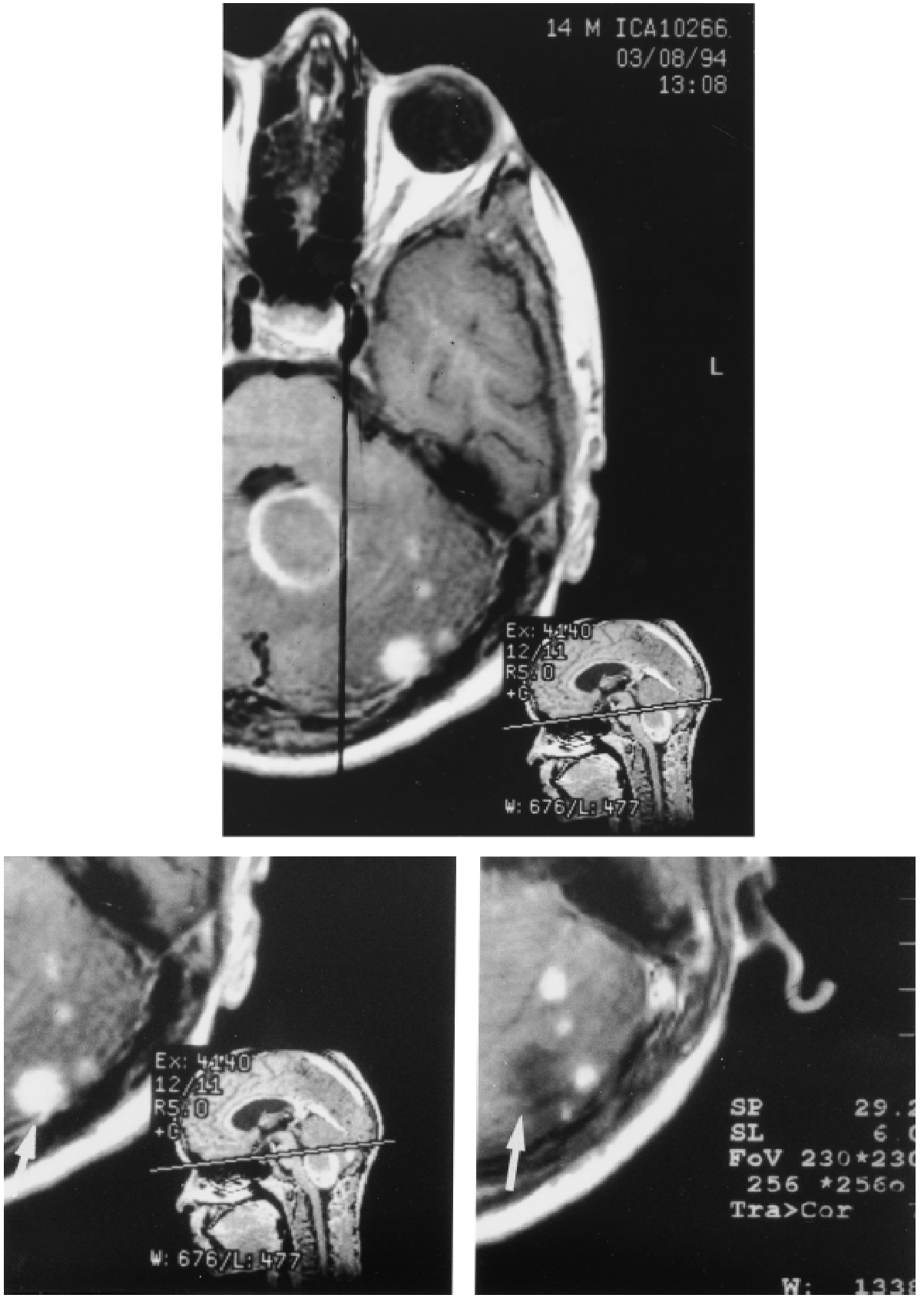

Fig. 1. Axial MRI of patient with multiple metachronous hemangioblastomas. **Top:** The presentation situation before surgery to the largest midline lesion. **Bottom:** The efficacy of radiosurgery on one of the persisting cerebellar tumors (arrows) (**left:** before; **right:** after).

Reply

We believe that the point made by Dr. Plowman properly highlights the potential role of radiotherapy for the treatment of patients affected by Von Hippel Lindau syndrome and multiple cerebral hemangioblastomas. The data available, as nicely reviewed by Dr. Plowman, show that conventionally fractionated radiotherapy as well as radiosurgery are clearly effective for this neoplasm. Because of the extreme phenotypic variability of the patients affected by this syndrome, particularly with regard to the occurrence of central nervous system hemangioblastomas, it is important to have clear in mind all of the treatment options available for them. Most of the time, in fact, therapy must be individually tailored to the specific clinical condition of the patient. Clearly, the treatment decision for benign central nervous system tumors could be as troublesome as the one for malignant neoplasms.

However, the suggestion made by Dr. Plowman about the systematic use of prophylactic external fractionated radiotherapy to the whole cerebellum for the treatment of multiple cerebellar hemangioblastomas after the radical removal of the large nodules ''to obliterate early and subclinical disease'' raises some concerns.

The main concern is related to the natural history of all the small and large enhancing nodules that the cerebral and spine MRI can show in these patients. Do they all have unequivocal growth potential, and if so, what is their growth rate? In other words, what does Dr. Plowman exactly mean by multiple cerebellar hemangioblastomas? Why should all of those enhancing nodules be irradiated d'émbleé at diagnosis? What is the disadvantage of waiting until they actually grow before treating them? In other words, what is the best time for treating them? None of the many enhancing nodules we saw at diagnosis in the spine and cerebral MRI of the girl we described in the proceedings has grown after 28 months of close follow-up [1]. If one accepted fully Dr. Plowman's proposal, considering that the case we described had multiple small enhancing nodules throughout the central nervous system, in the supratentorial regions as well as on the spine, one would be tempted to bring to the extreme the proposed recommendation, in this case craniospinal prophylactic radiotherapy. Furthermore, should an age limit be set for recommending this treatment? Finally, is the risk that radiotherapy may add a further danger to the tissues of patients suffering a cancer predisposing syndrome so trivial that we should not be worried about it?

We acknowledge that for some of these questions there are no precise answers, and one should rely on quite subjective considerations and on an often limited personal experience. This is definitely the case of the persons who write. It is hoped that centers of excellence for the treatment of this rare condition may soon achieve more visibility and consequently serve as referring centers for counseling on treatment intervention.

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